

71 acid selected from the group consisting of the amino acids of Reference (Table A, said polypeptide having at least one of the properties defined in claim 18.

72 49 (amended). A method of treating a disease which is treatable by a substance which has at least one of the following properties,

a) induces inhibition of spontaneous IL-8 production by human monocytes,

b) induces inhibition of IL-1 β induced IL-8 production by human peripheral blood mononuclear cells (PBMC),

c) induces production of interleukin-1 receptor antagonistic protein (IRAP) by human monocytes,

d) induces chemotactic migration of CD8+ human T lymphocytes in vitro,

e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,

f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,

g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,

h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN- γ ,

i) induces the production of IL-4 by cultured normal human CD4+ T cells,

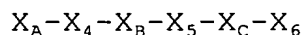
j) reduces the TNF α production in human mixed leukocyte reaction, or

k) downregulates TNF α and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits

which comprises administering to a subject in need thereof a pharmaceutically effective amount of a pharmaceutical composition according to claim 41.

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76 (amended). A non-naturally occurring polypeptide, or a polypeptide in at least partially purified form, which is six to 20 amino acids in length, and which comprises the following sequence



X_A is L-Thr or a non-natural or unusual amino acid,

X_B is L-Lys or a non-natural or unusual amino acid,

X_C is L-Arg or a non-natural or unusual amino acid,

X_4 and X_5 are independently selected from the group consisting of L-Met, L-Ile, L-Leu, L-Val and a non-natural or unusual amino acid,

X_6 is L-Asn, L-Asp, L-Gln, L-Glu, or a non-naturally or unusual amino acid,

no more than one of X_A , X_B , X_C , X_4 , X_5 and X_6 is a non-natural or unusual amino acid other than the D-isomer of an L-amino acid recited as possible at that position,

wherein at least one of the following conditions (I)-(V) is true:

I) at least one of X_A , X_B , X_C , X_4 , X_5 or X_6 is a non-natural or unusual amino acid,

II) the polypeptide is cyclized,

III) the polypeptide is stabilized,

IV) the aminoterminal amino acid residue is acylated, or

V) the carboxyterminal amino acid residue is amidated,

where, if the polypeptide is not cyclized, said sequence corresponds essentially to the C-terminal of said polypeptide, said polypeptide having at least one of the following properties:

a) induces inhibition of spontaneous IL-8 production by human monocytes,

b) induces inhibition of IL-1 β induced IL-8 production by human peripheral blood mononuclear cells (PBMC),

c) induces production of interleukin-1 receptor antagonistic protein (IRAP) by human monocytes,

d) induces chemotactic migration of CD8+ human T

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lymphocytes in vitro,

e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,

f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,

g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,

h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN- γ ,

i) induces the production of IL-4 by cultured normal human CD4+ T cells,

j) reduces TNF α production in human mixed leukocyte reaction, or

k) downregulates TNF α and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits, and wherein any non-natural or unusual amino acid referred to above is an amino acid set forth in reference table A.

REMARKS

1. Scope of Enablement/Non-Natural or Unusual AAs (OA \$4a)

The Examiner concedes enablement for peptides (of the claimed length) which comprise the following non-natural or unusual amino acids: norvaline, norleucine, N-methyl isoleucine, alloleucine, or any of the non-natural amino acids listed on page 18, but not for non-natural or usual amino acids generally.

The Examiner has considered our argument that other amino acids are listed in the three catalogues cited at page 18, lines 30 to page 19, line 2. However, the Examiner says that this material is then "essential material" for providing enablement for the claimed peptide but cannot be incorporated by reference as the catalogues are neither U.S. patents nor pending U.S.